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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,454	12/13/2006	Timothy Vollmer	68682-PCT-US/JPW/JW	1309

23432 7590 12/20/2010

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/20/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/556,454	VOLLMER, TIMOTHY	
	Examiner	Art Unit	
	MAURY AUDET	1654	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12/10/10 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Maury Audet/
Primary Examiner, Art Unit 1654

Continuation of 11. does NOT place the application in condition for allowance because:

Unamended claims 1-4,6-13,23-25,27-31 and 19-21 remain rejected for the reasons of record. Applicant's arguments After Final have been considered but are not persuasive. The claims remain rejected for the same reasons of record (see below): it would have been obvious (In re Kerkhoven type pattern) to administer to known products for their known purpose, and do so in combination, but with some time lag between administering the same (e.g. one substantially precedes the other (claim 1); or where one is administered 2-10 weeks after the other (claim 30); or where one is administered 2 weeks after the other and then given daily (claim 31)).

As to Applicant's assertion that the Examiner did not address new claims 30-31, this is also not persuasive. Claims 30-31 were addressed. They were listed as rejected under the same rationale as the original base claim/dependents thereof. The claims did not need to be addressed substantively in any way other than what was of record. The limitations of claims 30-31 are simply further random time element species of base claim 1. Time element limitations being known to be merely routinely optimizable by one of ordinary skill in the art, depending on the desired outcomes. UNLESS, a clear showing of unexpected results be shown.

Here, in claim 30-31, as in claim 1, Applicant has not provided by description or by argument in the latest round of respond, a clear showing of unexpected results, based on a staggered time administration, of two known compounds, for their known purpose.

Thus, the claimed invention remains obvious that the combination would be expected to produce some additive effect, or at least work as they normally would, in treating one or more symptoms of MS.

The rationale provided in the Final Rejection to Applicant's arguments is repeated below for continuity of record:

Applicant's arguments have been considered but are not found persuasive. The In re Kerkhoven fact pattern remains in the claims (administering two known products for their known use, together), and the 35 USC 103 rejection is maintained below; absent evidence to the contrary of test data showing administering mitoxantrone at some "substantially preceding" time before glatiramer acetate produces unexpected results in 1 or more MS symptoms v. a control group where both compounds are administered at/about the same time. Without this, either In re Kerkhoven applies that administration of known agents for a known use, in combination (even if not at the exact same time) would have predictable results OR since the agents are NOT actually being administered at the same time, then they are simply being separately administered, as the art already teaches both for (bordering on a 102 rejection based on the art record).

[ ]

Combination therapy in highly complex disorders such as MS, or even diabetes, is well known in the art.
The Examiner has fully considered the record:
1) Applicant's amendment and 105 page response;
2) The Exhibits of Volmer's 2008 article in MS; the MPEP section on 2143.02; the KSR and related caselaw;
3) each in the context of the claimed invention in view of the prior art combination; and can only conclude and maintain, not yet convinced by Applicant's arguments and evidence of record, that based the prior art combination, if not Szabo et al. alone, that one of ordinary skill in the art, using two known MS agents in combination (2 of 5 Szabo et al. taught/contemplated), would have had a reasonable expectation of success in treating MS by their combination, satisfying MPEP section 2143.02, as well as the recent case law guidance of and citing KSR.

[ ]

...invention directed to a therapy of known agents in combination for their known use, to somehow elicit something 'unexpected' (beyond merely synergistic effect, which would naturally be expected by administering two agents in combination, as Szabo et al. taught/suggested) - when the administration thereof is claimed essentially as "whenever" desired.

It is suggested that Applicant may wish to consider further review of any test data disclosed or evidence thereafter (e.g. via 1.132 Declaration) as to the metes and bounds of some specific amount/timeline regimen of both agents, that led Applicant's to believe they had stumbled upon a better combination therapy for those suffering from MS. Beyond the effect that would be expected by both known agents for their therapeutic benefit in MS sufferers, including beyond a mere synergistic effect.

The rejection is repeated below for continuity of record:
Szabo et al. teach "administering one or more additional agents for treating symptoms associated with multiple sclerosis") of glatiramer acetate and mitoxantrone (claim 11, as two of only five specifically contemplated "additional agents" also capable of treating multiple sclerosis) (see entire document, especially claims 10-11).

[ ]

II. Advisory Action & Previous Interview:
However, the Examiner also visits the substantive arguments in regards to the unamended claims, in order to advance prosecution, should Applicant consider the filing of an RCE/continuation application.
Under the broadest reasonably interpreation of the claims, the invention as claimed is not actually drawn to a combination, but rather administering A and then B PERIODICALLY, or vice versa (glatiramer acetate and mitoxantrone), which is not necessarily together (where there systemic amounts individually or collectively treat some 'symptom' of MS). Thus, any MS regimen - since often such is by trial & error - of administering at some point A and at some point B, or vice versa (e.g. periodically), reads on the invention as claimed.
Applicant may wish to consider in the future positively claiming both:
1. That A and B are co-administered or simultaneously administered; AND
2. The only symtpom discussed by argument as providing unexpected results based on THIS combination (beyond those symptoms A & B are recognized as treating individually)...A METHOD OF REDUCING THE NUMBER OF Gd-ENHANCING LESIONS (to a subject in need thereof, by co-administering A + B) (see page 3 of last response as to Applicant's discussion of unexpexcted results).
IF support is present in the specification, as relied upon in Applicant's later publication of results; in order to remove the presently maintained In re Kerkhoven fact pattern grounds of rejection under 35 USC 103.
In summary, Applicant's request for reconsideration and reliance upon various prior art references/opinions within the art (Exhibits), have been fully considered but are not found persuasive.
The 35 USC 103 rejection is maintained, the combination being deemed predictable as to success in treating MS (one or more of four standard forms).
The Examiner maintains reliance upon the rationale of In re Kerkhoven, that it would have been obvious to combine to known drugs for their known purpose (equivalents). It is noted that:
1. Additive effects do not traverse this grounds - without more, the results Applicants has provided on page 2-3 of 68 in the response (labeled unexpected), are presently deemed additive effects;
and; 2. Furthermore, even synergistic effects may be called into question, without further showing; since synergism is itself deemed unpredictable in the art..
Applicant's arguments that the FDA does not view any drug combinations as having predictable results is not deemed to obviate either of #1. or 2. above; as to the tests/case law applied in the determination of patentability. The Patent Office and the Food & Drug Administration operate under different standards, which are not necessarily applicable to the other, in the determination of patentable subject matter versus safe-for-public use foods/drugs.
2144.06 [R-6] Art Recognized Equivalence for the Same Purpose
>1. COMBINING EQUIVALENTS KNOWN FOR THE SAME PURPOSE
"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose .... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). **
The Examiner copies the previous Interview Summary for continuity of record:
Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicant telephoned to discuss the outstanding 35 USC 103 rejection in the Final Rejection. Applicant's position is that the issue rests on whether the combination of art applied would have rendered the claimed invention predictable, with a reasonabe expectation of success.
The prior art does not teach using the specific combination of known MS drugs, for their known purpose:
1. The 1st compound Glatiramer acetate is well known in MS therapy (reference of record);
2. The 2nd compound, Mitoxantrone, the Kerwar reference teaches or suggests for use for treating MS, alone.
Applicant indicates that, as for MS combinations, they have filed 1 reference casting doubt on the predictability of combinations - at least as to additive effect (e.g. the combination had no greater effect). The Examiner indicated that the test for obvoiusness for using two known compounds for their known use, is not whether the art has shown something less then a synergistic effect (which in itself by testing, may not be enough to even overcome an obviousness rejection).
I. Applicant then indicated they are submitting 2 new references that show even reduced effect with combinations of known MS drugs. Applicant's position being that they have rebutted the prima facie case and that unpredictability is present.

II Secondly, Applicant reiterated the FDA's position, that they made of record, that combinations of known drugs for their known uses are 'generally' unpredictable under FDA guidelines. The Examiner indicated the USPTO follows

separate guidelines [e.g. In re Kerkhoven] from the FDA; but that the relevance of this statement in the context of the other evidence will be fully reviewed.
III. Thirdly, and most importantly the Examiner noted, Applicant will be reviewing the test data from this combination to
determine if in fact a synergistic, as opposed to merely additive, effect was shown by this combination.
Applicant will be filing the response with the above shortly, which will be fully considered by the Examiner.